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REMARKS

Reconsideration of the present application is respectfully requested. Claims 2-10, 12, 14, and 15 are pending. Claim 13 has been cancelled without prejudice. Support for these claims is found in the claims as originally filed, and throughout the specification. No new matter has been added.

The Examiner has objected to the amended title "Rad51-Like Orthologues and Uses Thereof" stating that it is not descriptive of the instant invention drawn to a RAD51 gene, not to the protein. Applicants presume the term objected to in the title is "orthologue" and respectfully disagree that this is not a proper descriptive term. However, in order to expedite prosecution, Applicants have amended the title to replace the term "orthologues" with the term "polynucleotides". Applicants believe this amendment obviates the objection and respectfully request this objection be withdrawn, or if the objection has been misinterpreted, that the Examiner clarify by specifically identifying the objectionable term or phrase.

Claims 8, 9, 12, 14 and 15 have been amended.

Claim 8 has been amended to make explicit what was implicit in the original claim. Specifically, as amended claim 8 recites "wherein the seed comprises the recombinant expression cassette".

Claims 9, 12, 14 and 15 have been amended to correct informalities regarding improper definite articles.

Claim 12 has been amended to recite "wherein the polynucleotide of (a), (b), (c), or (d) modulates the level of Rad51C polypeptide". Claims 14 and 15 have also been amended to recite this function. Support for this amendment can be found on page 23, lines 6-11 and page 54, line 29 – page 56, line 2 of the specification and in the claims as originally filed.

Claim 14 has been amended to make explicit what was implicit in the original claim. Specifically, as amended claim 14 recites specific high stringency

hybridization conditions. Support for this amendment can be found on page 16, lines 11-13 of the specification.

The marked up version of these amendments is found on a separate sheet attached to this amendment and titled **"Version with Markings to Show Changes Made."** It is respectfully requested that the amendments be entered.

Rejections under 35 U.S.C. §101:

Claim 14 is rejected under 35 U.S.C. §101 as not having either a credible asserted utility or a well-established utility.

The Examiner asserts that isolated polynucleotides of at least 100 contiguous nucleotides that selectively hybridize to SEQ ID NO: 1 include a human DNA repair protein (1998, GenBank AI184177), and that the instant specification does not teach a specific use of these nucleic acids.

Claim 14 has been amended to recite "wherein stringent hybridization conditions comprise 50% formamide, 1M NaCl, and 1% SDS at 37°C, or conditions equivalent thereto, wherein the polynucleotide modulates the level of Rad51C polypeptide". As amended, the claim does require utility as disclosed in the specification. This amendment obviates the rejection.

Further, the amended claim does not encompass a human DNA repair protein with no disclosed use. The amended claim recites specific, high stringency hybridization conditions, page 15, lines 1-3 of the specification notes that "Selectively hybridizing sequences typically have about at least 80% sequence identity, preferably 90% sequence identity, and most preferably 100% sequence identity (i.e., complementary) with each other." The sequence disclosed in GenBank AI184177 does not have 100 contiguous nucleotides which share at least 80% sequence identity with SEQ ID NO: 1, therefore will not selectively hybridize under the conditions listed in the amended claim.

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The Examiner maintains the rejection of claim 8 under 35 U.S.C. §101 as not having a specific or well-established utility because the claim does not require that the transgenic seed have the expression cassette of claim 2.

Claim 8 has been amended, as recommended by the Examiner, to recite "wherein the seed comprises the recombinant expression cassette". This amendment obviates the rejection.

Applicants have properly addressed the grounds for the rejection of claims 14 and 8 under 35 U.S.C. §101 and respectfully request that the rejection of the claims under 35 U.S.C §101 be withdrawn.

Rejections under 35 U.S.C. §112, first paragraph – Utility:

Claim 14 is rejected under 35 U.S.C. §112, first paragraph as the claimed invention lacks utility, therefore one of skill in the art would not know how to use the invention.

As the Applicants have responded to the utility rejection under 35 U.S.C. §101, it is believed that the utility rejection has been overcome. As amended the claim requires utility, the polynucleotide "modulates the level of Rad51C polypeptide". Therefore, it is respectfully requested that the concomitant rejection of claim 14 under 35 U.S.C. §112, first paragraph based on a lack of utility be withdrawn.

Rejections under 35 U.S.C. §112, first paragraph:

The Examiner states "Claims 2-10 and 12-15 are rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for nucleic acids of SEQ ID NO: 1 or that encode SEQ ID NO: 2, does not reasonably provide enablement for nucleic acids that have 80% identity to SEQ ID NO: 1, that are amplified from primers that hybridize under unspecified stringency to 'loci within' SEQ ID NO: 1, or that comprise 100 nucleotides that hybridize to SEQ ID NO: 1."

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As is stated in MPEP 2164.01 "A patent need not teach, and preferably omits, what is well known in the art. *In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987); and *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1463, 221 USPQ 481, 489 (Fed. Cir. 1984)."

Further, Applicants submit that the specification is not required to disclose all possible permutations as defined by the limitations of the claims. The specification is required to provide sufficient disclosure and enablement so that one skilled in the art could make the embodiments encompassed by the claims. "It is well settled that patent applicants are not required to disclose every species encompassed by their claims, even in an unpredictable art . . ." *In re Vaek*, 947 F.2d 488; 20 USPQ2d 1438 (Fed. Cir. 1991).

As pointed out in the response filed 15 April, 2002, the present application and the knowledge in the art provides sufficient information and guidance to enable one of skill in the art to make and use a polynucleotide with at least 80% sequence identity to SEQ ID NO: 1, or that selectively hybridizes to SEQ ID NO: 1 under the stringent conditions presented in amended claim 14. The disclosure does not teach the "mere germ of an idea", the disclosure teaches three independent full length Rad51C polynucleotide sequences and teaches one of skill in the art methods to isolate, make, modify and identify polynucleotides with 80% sequence identity to SEQ ID NO: 1, or that selectively hybridize to SEQ ID NO: 1 under the proscribed conditions. While the Examiner dismisses the extensive guidance in the specification pointed to in the response filed 15 April 2002 as "general", this guidance is sufficient to enable one of skill in the art to readily make the embodiments encompassed by the claims.

The Examiner asserts that undue experimentation would have been required by one skilled in the art to practice the invention. The Examiner contends one would

have to make all the possible single amino acids substitutions and analyze the greater than 19^{294} nucleic acids generated. The Examiner also asserts undue trial and error would be required to screen through all the plants transformed with the polynucleotides encompassed by the present invention.

The Applicants respectfully disagree. It is not necessary to make and assay every possible substitution in order to obtain a polynucleotide that modulates the level of Rad51C polypeptide, one or a few variants will suffice. The question of experimentation is a matter of degree. The fact that some experimentation is necessary does not preclude enablement; what is required is the amount of experimentation must not be unduly extensive. *PPG Inc. v. Guardian Industries Corp.* (37 USPQ 1218, 1623, (Fed. Cir. 1996). The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed. *Ex parte Jackson*, 217 USPQ 804, 807 (1982 PTOBA).

Claims 12, 14 and 15 have been amended to claim polynucleotides "which modulate the level of Rad51C polypeptide". As noted above, Applicants have disclosed several sequences (SEQ ID NOS: 1-6), provided guidance regarding modifications to the sequences, methods to analyze, isolate, identify and characterize the sequences. The 3-dimensional structure of related proteins were known in the art at the time of filing, as well as methods to assay for functional RAD51 homologues. Although techniques for expressing, monitoring, and purifying polypeptides are well-known in the art, additional disclosure can be found on pages 29–31, pages 46-49, and page 52 of the specification. Therefore screening for the polynucleotides and polypeptides of the present invention, either structurally or functionally, is routine experimentation.

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Applicants have provided reasonable guidance such that one of skill in the art can practice the breadth of the invention as disclosed and claimed, therefore the rejection of claims 2-10 and 12-15 under 35 U.S.C. §112, first paragraph should be withdrawn.

Claims 2-10 and 12 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant are that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to specific polynucleotides having a predictable structure represented by their sequence identity to SEQ ID NO: 1. In this way, Applicants have conceived the sequences of the invention as articulated in *Amgen v. Chugai Pharm.*; that is, Applicants are able "to envision the detailed constitution of a gene so as to distinguish it from other materials, as well as a method for obtaining it." *Amgen, Inc. v. Chugai Pharm. Co.*, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991), *cert. denied*, 112 S. Ct. 169 (1991).

The polynucleotide claims further recite a functional characteristic, that they modulate the level of Rad51C polypeptide. The written description requirement may also be satisfied by a recitation of functional characteristics. For example, on page 53 of the *Revised Interim Written Description Guidelines*, Example 14 is directed to a generic claim of a protein having high sequence identity to the sequence of SEQ ID NO: 3, "wherein the sequence catalyzes the reaction A -> B." The Guidelines concludes that the generic claim of Example 14 is sufficiently described under §112, first paragraph because:

1) the single sequence disclosed in SEQ ID NO: 3 is representative of the genus, and

2) the claim recites a limitation requiring the compound to catalyze the reaction from A-> B.

Thus, on the basis of the limitations provided in Example 14, one of skill in the art would recognize that the patentee was in possession of the necessary common attributes possessed by the members of the genus. In the instant case, the amended claims all require the functional limitation that the claimed polynucleotides modulate the level of Rad51C polypeptide.

Applicants have sufficiently described by way of structural, chemical, and functional characteristics the polynucleotides of the present invention to reasonably convey to one of skill in the art that the Applicants were in possession of the invention at the time of filing.

The Examiner states: "Neither the instant specification nor the originally filed claims appear to provide support for the phrase 'over the entire length of the reference sequence' in claim 12." Applicants point to page 17, line 32 – page 18, line 2 and page 20, lines 8-10 of the specification, which support the use of this phrase. Therefore, this phrase does not constitute new matter.

In light of the amendments and arguments presented above, Applicants respectfully request that the rejection of claims 2-10 and 12, 14 and 15 under 35 U.S.C §112 first paragraph be withdrawn.

Rejections under 35 U.S.C. §112, second paragraph:

Claims 2-10 and 12-14 have been rejected under 35 U.S.C. § 112, second paragraph as being indefinite.

Claim 13 has been cancelled without prejudice. Claim 14 has been amended to recite specific high stringency hybridization conditions. As stated in the response filed 15 April, 2002, the term "selectively hybridizes" is defined in the specification. Coupled with the recitation of specific stringent hybridization conditions, Applicants believe the claim is definite. The role of wash conditions is discussed on pages 16-17. While temperature and ionic strength are viewed as important factors, the time of the wash, in general is not. Claim 14 defines the *important* wash parameters of

ionic strength and temperature as 0.1X SSC at 60°C. Ausubel, *et al.* review the important parameters for hybridization in chapter 2.10 of Volume 1 *Current Protocols in Molecular Biology* (1995, Greene Publishing and John Wiley and Sons). In particular, see pages 2.10.8 – 2.10.15 which review the parameters important to sensitivity and specificity and provides a troubleshooting guide. As is stated on page 2.10.10, column 2, paragraph 2 "Specificity is the function of post-hybridization washes, the critical parameters being the ionic strength of the final wash solution and the temperature at which this wash is carried out." Further discussion regarding troubleshooting lack of specificity point to changing the ionic strength, or the temperature at which the wash is done, not the time of the wash. Therefore, Applicants believe recitation of a particular time for which the wash is done is unnecessary.

Applicant has addressed the rejections under 35 U.S.C. §112, second paragraph by proper amendments and arguments. Claims 2-15 are in proper form, therefore Applicant respectfully requests the rejections under 35 U.S.C. §112, second paragraph be withdrawn.

Rejections under 35 U.S.C. § 102:

Claim 14 is rejected under 35 U.S.C. §102(a) as being anticipated by NCI-CGAP (1998, GenBank Accession No. AI184177) for reasons of record. The Examiner asserts the nucleic acid taught by NCI-CGAP would selectively hybridize to SEQ ID NO: 1.

Claim 14 has been amended and now explicitly recites high stringency hybridization conditions. Page 15, lines 1-3 of the specification notes that "Selectively hybridizing sequences typically have about at least 80% sequence identity, preferably 90% sequence identity, and most preferably 100% sequence identity (i.e., complementary) with each other." The sequence disclosed in GenBank AI184177 does not have 100 contiguous nucleotides which share at least 80%

sequence identity with SEQ ID NO: 1. The nucleic acid taught by NCI-CGAP would not selectively hybridize to SEQ ID NO: 1 under these conditions as discussed above, thereby obviating the rejection.

Applicants respectfully request that the rejection of claim 14 under 35 U.S.C. § 102(a) be withdrawn.

CONCLUSION

In light of the foregoing remarks and amendments, withdrawal of the outstanding rejections and allowance of all of the remaining claims is respectfully requested. Applicants believe that the claims are in condition for allowance. The Examiner is invited to telephone the Applicant in order to expedite prosecution of the application.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

The Applicants have used underlining to denote additions to the original text and square brackets [ ] to denote deletions of the original text.

In the Title:

The title found on the cover page has been amended as follows:

Rad51-Like [Orthologues] Polynucleotides and Uses Thereof

In the Claims:

Claim 13 has been cancelled.

Claims 8, 9, 12, 14 and 15 have been amended as follows:

8. (Amended) A transgenic seed from the transgenic plant of claim 4, wherein the seed comprises the recombinant expression cassette.

9. (Twice Amended) A method of modulating the level of RAD51C in a plant, comprising:
   (a) introducing into a plant cell a recombinant expression cassette comprising [a] the polynucleotide of claim 12 operably linked to a promoter;
   (b) culturing the plant cell under plant cell growing conditions;
   (c) regenerating a whole plant which possesses the transformed genotype; and

(d) inducing expression of said polynucleotide for a time sufficient to modulate the level of RAD51C in said plant.

12. (Amended) An isolated polynucleotide [encoding a polypeptide with Rad51C activity comprising a member] selected from the group consisting of:

(a) a polynucleotide having at least 80% sequence identity over the entire length of the reference sequence, as determined by the GAP program under default parameters, to [a] the polynucleotide of SEQ ID NO: 1;

(b) a polynucleotide encoding [a] the polypeptide of SEQ ID NO: 2;

(c) a polynucleotide of SEQ ID NO: 1;

(d) a polynucleotide which is fully complementary to [a] the polynucleotide of (a), (b), or (c);

wherein the polynucleotide of (a), (b), (c), or (d) modulates the level of Rad51C polypeptide.

14. (Amended) An isolated polynucleotide comprising at least 100 contiguous nucleotides which selectively hybridizes, under stringent hybridization conditions and a wash in 0.1X SSC at 60°C, to [a] the polynucleotide of SEQ ID NO: 1, wherein stringent hybridization conditions comprise 50% formamide, 1M NaCl, and 1% SDS at 37°C, or conditions equivalent thereto, and wherein the polynucleotide modulates the level of Rad51C polypeptide.

15. (Amended) An isolated polynucleotide comprising at least 50 contiguous nucleotides from [a] the polynucleotide of SEQ ID NO: 1, wherein the polynucleotide modulates the level of Rad51C polypeptide.